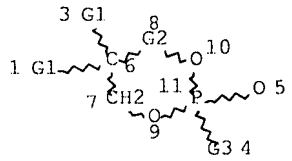
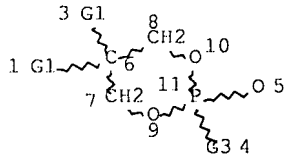
STRUCTURE SEARCH

```
=> d his l43

     (FILE 'HCAPLUS' ENTERED AT 17:23:57 ON 15 OCT 2007)
                SAV L42 SHI490HCP/A
L43            4 S L42 NOT L39

=> d que l43
L2            36 SEA FILE=REGISTRY ABB=ON  PLU=ON  (100-39-0/BI OR
                 100-51-6/BI OR 107-88-0/BI OR 108-01-0/BI OR 124613-28-
                 1/BI OR 126-11-4/BI OR 13507-10-3/BI OR 142-62-1/BI OR
                 14690-00-7/BI OR 16727-61-0/BI OR 187976-16-5/BI OR
                 2163-42-0/BI OR 22102-92-7/BI OR 26362-71-0/BI OR
                 3443-84-3/BI OR 459-73-4/BI OR 504-63-2/BI OR 52066-54-
                 3/BI OR 52692-02-1/BI OR 534-03-2/BI OR 600174-74-1/BI
                 OR 600174-75-2/BI OR 600174-76-3/BI OR 600174-77-4/BI
                 OR 600174-78-5/BI OR 600174-79-6/BI OR 600174-80-9/BI
                 OR 600174-81-0/BI OR 600174-82-1/BI OR 600174-83-2/BI
                 OR 600174-84-3/BI OR 64821-66-5/BI OR 68755-22-6/BI OR
                 77-86-1/BI OR 872-99-1/BI OR 88946-00-3/BI)
L4               STR
```

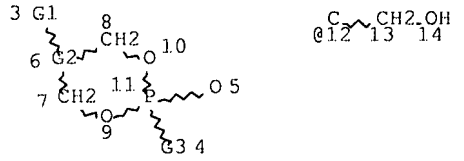



```
VAR G1=H/N/O/C
REP G2=(0-1) CH2
VAR G3=N/O
NODE ATTRIBUTES:
CONNECT IS E1  RC AT   5
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  10

STEREO ATTRIBUTES: NONE
L5          2404 SEA FILE=REGISTRY SSS FUL L4
L6               STR
```




```
VAR G1=H/N/O/C
VAR G3=N/O
NODE ATTRIBUTES:
CONNECT IS E1  RC AT   5
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
```

```
RSPEC I
NUMBER OF NODES IS  10

STEREO ATTRIBUTES: NONE
L8          1420 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L10              STR
```



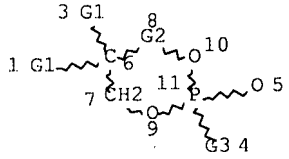

```
VAR G1=H/N/O/C
VAR G2=CH/12
VAR G3=N/O
NODE ATTRIBUTES:
CONNECT IS E1  RC AT   5
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  12

STEREO ATTRIBUTES: NONE
L12          539 SEA FILE=REGISTRY SUB=L8 SSS FUL L10
L13           16 SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 AND L2
L16           54 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13
L17          757 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8
L18          399 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12
L19              QUE  ABB=ON  PLU=ON  NERVE+PFT,OLD,NT/CT
L20              QUE  ABB=ON  PLU=ON  NEURON+PFT,OLD,NT/CT
L21              QUE  ABB=ON  PLU=ON  NERV? OR NEURON? OR AXON?
L22            8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17 AND ((L19 OR L20
                 OR L21))
L24              QUE  ABB=ON  PLU=ON  L21(3A)(GROW? OR STIMUL? OR ACTIVA
                 T? OR PROMOT?)
L25            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17 AND L24
L26            8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L25 OR L22
L27              QUE  ABB=ON  PLU=ON  PY<2003 OR PRY<2003 OR AY<2003 OR
                 MY<2003 OR REVIEW/DT
L28            7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L26 AND L27
L31              QUE  ABB=ON  PLU=ON  "YEDA RES?"/PA,CS,SO,CO
L32          211 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("SHINITSKY M"/AU OR
                 "SHINITSKY MEIR"/AU OR "SHINITZKY M"/AU OR "SHINITZKY
                 MEIR"/AU)
L33            9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L32 AND L17
L34           25 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L32 AND L31
L35           29 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L33 OR L34
L36           27 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L35 AND L27
L37            6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 AND ((L19 OR L20
                 OR L21) OR L24)
L38            7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L33 AND L27
L39           10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L37 OR L38
L40            8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ((L16 OR L17 OR L18))
                 AND ((L19 OR L20 OR L21))
L41            7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L40 AND L27
L42            7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L41 OR L28
L43            4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L42 NOT L39


=> d his l53
```

(FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 17:43:02 ON 15 OCT 2007)

L53 18 S L45 NOT L52

=> d que stat l53

L4 STR



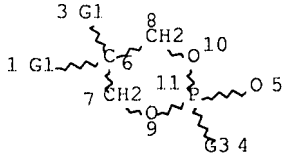
VAR G1=H/N/O/C
REP G2=(0-1) CH2
VAR G3=N/O
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 5
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

L5 2404 SEA FILE=REGISTRY SSS FUL L4

L6 STR



VAR G1=H/N/O/C
VAR G3=N/O
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 5
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

L8 1420 SEA FILE=REGISTRY SUB=L5 SSS FUL L6

L15 5 SEA FILE=REGISTRY ABB=ON PLU=ON L8 AND (MEDLINE/LC OR BIOSIS/LC OR DRUGU/LC OR EMBASE/LC)

L21 QUE ABB=ON PLU=ON NERV? OR NEURON? OR AXON?

L27 QUE ABB=ON PLU=ON PY<2003 OR PRY<2003 OR AY<2003 OR MY<2003 OR REVIEW/DT

L30 QUE ABB=ON PLU=ON ("SHINITSKY M"/AU OR "SHINITSKY MEIR"/AU OR "SHINITZKY M"/AU OR "SHINITZKY MEIR"/AU)

L31 QUE ABB=ON PLU=ON "YEDA RES?"/PA,CS,SO,CO

L44 20 SEA L15

L45 19 SEA L44 AND L27

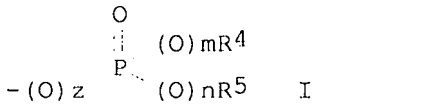
L1 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:224038 CAPLUS
DOCUMENT NUMBER: 126:212447
TITLE: Phosphorous-containing dipeptide inhibitors of cysteine and serine protease
INVENTOR(S): Mallamo, John P.; Bihovsky, Ron; Tao, Ming; Wells, Gregory J.
PATENT ASSIGNEE(S): Cephalon, Inc., USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9703679	A1	19970206	WO 1996-US11625	19960712
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
US 5639732	A	19970617	US 1996-679342	19960710
CA 2226414	A1	19970206	CA 1996-2226414	19960712
AU 9664583	A	19970218	AU 1996-64583	19960712
EP 871454	A1	19981021	EP 1996-923756	19960712
EP 871454	B1	20031112		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11509231	T	19990817	JP 1996-506762	19960712
AT 253920	T	20031115	AT 1996-923756	19960712
EP 1389624	A1	20040218	EP 2003-78371	19960712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PT 871454	T	20040331	PT 1996-923756	19960712
ES 2210377	T3	20040701	ES 1996-923756	19960712
HK 1016495	A1	20040813	HK 1999-101617	19990414

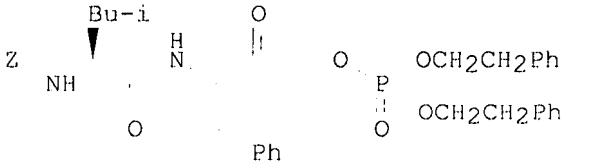
PRIORITY APPLN. INFO.:

US 1995-1491P	P	19950717
US 1996-679342	A	19960710
EP 1996-923756	A3	19960712
WO 1996-US11625	W	19960712

OTHER SOURCE(S): MARPAT 126:212447
GI



I



II

AB The present invention is directed to novel phosphorous-containing inhibitors of cysteine or serine proteases of the formula X-W-Y-CH(R2)-CO-NH-CH(R1)-CO-[CH(R3)]t-Q wherein: X = e.g., C6-C14 aryl, heteroaryl with C6-C14 ring atoms, C1-C10 alkyl (un) substituted with one or more J groups, C1-C10 alkoxy; W = CO, SO2; Y = NH, (CH2)k where k = 0-3; R1 and R2 are independently, e.g., H, C1-C14 alkyl (un) substituted with one or more J groups, C3-C10 cycloalkyl (un) substituted with one or more J groups; R3 = e.g., H, lower alkyl, aryl, heteroaryl; t = 0 or 1; Q = I wherein m, n, and z are independently 0 or 1; R4 and R5 are independently, e.g., H, lower alkyl (un) substituted with J, heteroaryl (un) substituted with J, or taken together to form a 5-8 membered heterocyclic ring (un) substituted with J; J = e.g., halogen, alkyl, guanidino, alkoxy. Thus, e.g., substitution reaction of Z-Leu-Phe-CH2Br with bis(phenethyl)phosphate afforded dipeptide derivative II (Z = PhCH2O2C) in 62% yield which exhibited 99% inhibition of calpain I at 0.1 μM. Methods for the use of the protease inhibitors are also described.

IT 187976-16-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phosphorous-containing dipeptide inhibitors of cysteine and serine protease)

RN 187976-16-5 CAPLUS

CN 1,3,2-Dioxaphosphorinane, 2-hydroxy-5-(phenylmethoxy)-, 2-oxide (9CI) (CA INDEX NAME)